ChemPubSoc Europe

DOI: 10.1002/chem.201501152

CHEMISTRY A European Journal Full Paper

Cobalt Catalysis

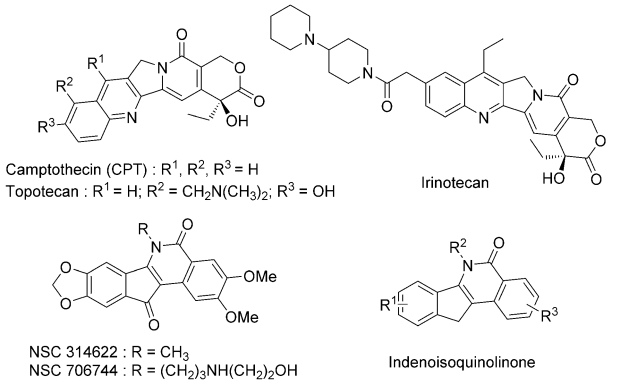
Cobalt-Catalyzed Dual Annulation of *o*-Halobenzaldimine with Alkyne: A Powerful Route toward Bioactive Indenoisoquinolinones

Chuan-Che Liu,[a] Jen-Chieh Hsieh,*[b] Rajendra Prasad Korivi,[a] and Chien-Hong Cheng*[a]

Abstract: A cobalt-catalyzed dual annulation reaction for the synthesis of variously substituted indenoisoquinolinones from 2-bromobenzaldehydes, amines, and methyl 2-(ethynyl)benzoates has been developed. This method could also be applied to the synthesis of an array of highly functionalized bioactive indenoisoquinolinones and their derivatives. A possible mechanism of the cobalt catalysis is proposed, involving imine formation from bromobenzaldehyde and the amine, followed by a series of oxidative addition, alkyne insertion, cyclization reactions, and carbon–carbon double-bond migration. The regioselective alkyne insertion plays an important role for the success of the second annulation.

Introduction

Camptothecin (CPT) and its analogues (Scheme 1) are important DNA topoisomerase I (Top I) inhibitors, which display marked cytotoxic properties and are FDA-approved medication for cancer treatment.[1] However, some problems associated with their usage have been found. For example, the binding complex (DNA–CPT–Top I) formed is reversible after the drug was removed.[1] Recently, several indenoisoquinoline-diones have shown a similar DNA cleavage pattern with good chemical stability and resistance to reversal after the drug was removed (NSC 706744, NSC 314622 etc).[2] In addition, indenoisoquinolinones were found to be useful in treating inflammatory diseases as well. Previous reports for the synthesis of indenoisoquinoline-diones mainly relied on the condensation reaction between the homophthalic anhydride and the imine to prepare a 3,4-disubstituted isoquinolinone-carboxylic acid and this was later converted to the indenoisoquinolinone by a cyclization reaction.[3] Unfortunately, this method gave a mixture of *cis* and *trans* isomers, but only the *cis* isomer is suitable for the cyclization reaction. Moreover, the preparation of substrates is tortuous and a multistep synthesis is required.[3] Cyclization of the lithiated toluamide with nitriles was also reported to be a strategy for the synthesis of indenoisoquinoline-diones; however, the process is still complicated with limitation of the substrate scope.[3f] Also, there is no direct procedure for the synthesis of indenoisoquinolinones, which were generally prepared by a reduction of the corresponding indenoisoquinoline-dione followed by a dehydration reaction by using triethylsilane and trifluoroacetic acid.[3c]



Scheme 1. Camptothecin and its analogues, bioactive indenoisoquinoline-diones, and indenoisoquinolinones.

Results and Discussion

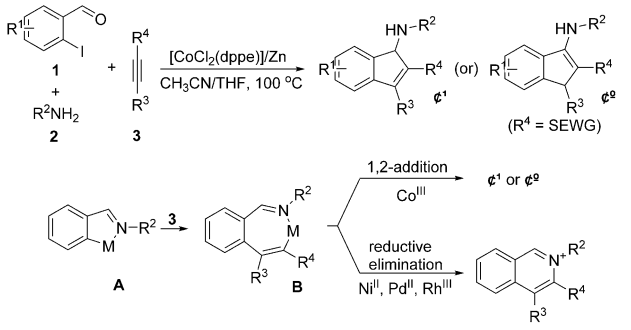
Recently, we observed the cyclization of *o*-halobenzaldimines with alkynes in the presence of cobalt complexes to give indenamine products, regioselectively.[4a] The Indenamine derivative **I** was obtained if the loaded alkyne did not contain an electron-withdrawing group. On the other hand, the indenamine **II** with a double-bond migration was found if the alkyne had a strong electron-withdrawing substituent (R^4 = strong electron-withdrawing group (SEWG), Scheme 2).

The results are in sharp contrast to the nickel-,[4b–d] palladium-,[4e–h] and rhodium-catalyzed[4i–k] formation of isoquinolinium salts from *o*-halobenzaldimines and alkynes. The formation

[a] *Dr. C.-C. Liu, Dr. R. P. Korivi, Prof. Dr. C.-H. Cheng*
Department of Chemistry
National Tsing Hua University
Hsinchu 30013 (Taiwan)
E-mail: chcheng@mx.nthu.edu.tw

[b] *Prof. Dr. J.-C. Hsieh*
Department of Chemistry
Tamkang University
New Taipei City, 25137 (Taiwan)
E-mail: jchsieh@mail.tku.edu.tw

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.201501152.



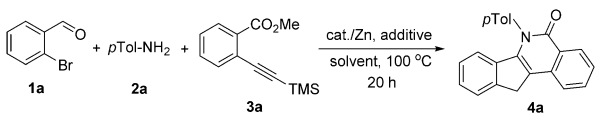
Scheme 2. Metal-selective syntheses of indenamines and isoquinolines from the azacomplex **A**. dppe = 1,2-bis(diphenylphosphino)ethane.

of indenamine **II** prompted us to explore the possibility for the application of this cobalt catalysis to the synthesis of indenoisoquinolinones. Herein, we report a one-pot synthesis of indenoisoquinolinones from *o*-halobenzaldimines by using cobalt complexes as catalysts. This catalytic reaction demonstrates a new tandem nucleophilic addition of vinylcobalt species to imine and carbonyl groups. The method can be applied to the synthesis of biologically active indenoisoquinoline derivatives with much shorter synthetic steps compared to previous reports.[3]

We envisioned that, in the cobalt-catalyzed synthesis of indenamine derivative, if the alkyne used has an ester group at the *ortho* position of the aryl substituent, further reaction of the coordinated amide group with the ester group is likely to provide a unique access to substituted indenoisoquinolinones (see the mechanism for details). To test this possibility, we prepared substrate **3a** through a Sonogashira coupling reaction of trimethylsilylacetylene with methyl *o*-iodobenzoate. The reaction of *o*-bromobenzaldehyde (**1a**) and *p*-tolylamine (**2a**) with compound **3a** in the presence of [$CoCl_2$(dppe)] and zinc metal powder gave the expected indenoisoquinolinone derivative **4a** in very low yield (Table 1, entry 1). We then examined the effect of various cobalt complexes, ligands, and Lewis acid additives. It was found that the reaction was completely inhibited when extra acetylacetonate (acac) was loaded to the solution. The desired product **4a** was obtained in slightly better yield when [$CoCl_2$(dppe)] was used along with extra dppe and further improvement was observed when $ZnCl_2$ was added into the reaction mixture (Table 1, entries 3 and 4).

Under the same reaction conditions, using [CoI_2(dppf)] (dppf = 1,1′-bis(diphenylphosphino)ferrocene) as the catalyst, the reaction provided product **4a** in 23% yield; however, compared to [CoI_2(dppe)], the crude NMR spectrum of the reaction mixture revealed that no other side products were formed. Hence, [CoI_2(dppf)] was chosen for further investigations. Significant improvement was realized when the quantity of the imine components **1a** and **2a** were increased with respect to the alkyne (**1a**/**2a**/**3a** = 2:2:1, Table 1, entry 7). The addition of 200 mol% of $ZnCl_2$ led to further improvement and a much better result was realized when the reaction was carried out in CH_3CN (Table 1, entries 8 and 9). However, when 300 mol% of $ZnCl_2$ were used, a lower yield of compound **4a** was observed (Table 1, entry 10). It is interesting to note that the formation

Table 1. Optimization studies for the synthesis of indenoisoquinolinone **4a**.[a]



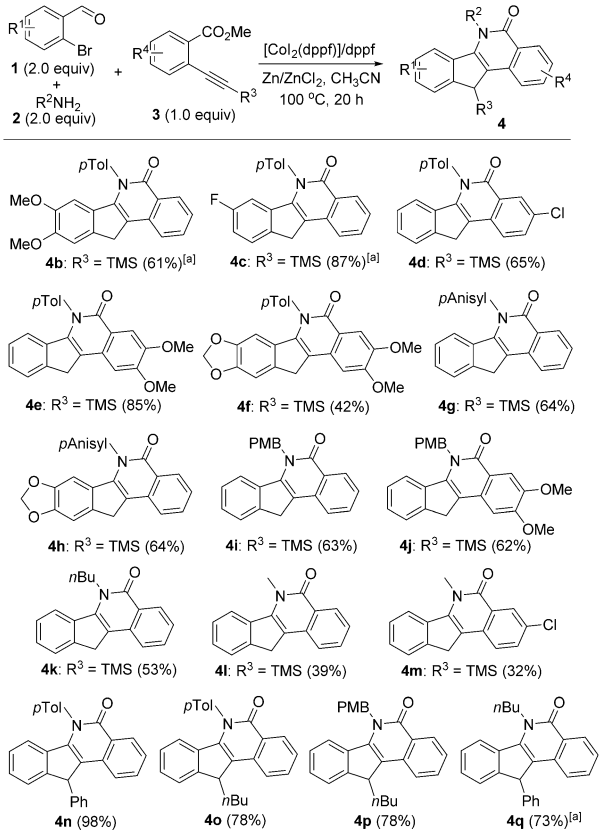
Entry	Catalyst/ligand (1:1)	Additive	Solvent (ratio)	Yield [%][b]
1[c]	[$CoCl_2$(dppe)]/none	none	CH_3CN/THF (1:1)	9
2[c]	[$CoCl_2$(dppe)]/acac	none	CH_3CN/THF (8:2)	0
3[c]	[$CoCl_2$(dppe)]/dppe	none	CH_3CN/THF (8:2)	13
4[c,e]	[$CoCl_2$(dppe)]/dppe	$ZnCl_2$	CH_3CN/THF (1:1)	22
5[c,e]	[CoI_2(dppf)]/dppf	$ZnCl_2$	CH_3CN/THF (1:1)	23
6[d]	[CoI_2(dppf)]/dppf	none	CH_3CN/THF (1:1)	12
7[d,e]	[CoI_2(dppf)]/dppf	$ZnCl_2$	CH_3CN/THF (1:1)	68
8[d,f]	[CoI_2(dppf)]/dppf	$ZnCl_2$	CH_3CN/THF (1/1)	75
9[d,f]	[CoI_2(dppf)]/dppf	$ZnCl_2$	CH_3CN	92
10[d,g]	[CoI_2(dppf)]/dppf	$ZnCl_2$	CH_3CN	60

[a] Reaction conditions: *o*-bromobenzaldehyde, *p*-toluidine, alkyne, cobalt complex (0.021 mmol), ligand (0.021 mmol), and Zn (0.6 mmol) in solvent (1 mL) at 100 °C for 20 h. [b] NMR spectroscopic yields by using mesitylene as an internal standard. [c] Ratio of reactants: **1a**/**2a**/**3a** = 0.3:0.3:0.6 mmol. [d] Ratio of reactants: **1a**/**2a**/**3a** = 0.6:0.6:0.3 mmol. [e] $ZnCl_2$: 0.3 mmol. [f] $ZnCl_2$: 0.6 mmol. [g] $ZnCl_2$: 0.9 mmol.

of the indenoisoquinolinone **4a** involves three tandem steps: cobalt-catalyzed formation of the indenamine core, formation of the C–N bond, carbon–carbon double-bond migration, and removal of the trimethylsilyl (TMS) group under the present reaction conditions.

The cobalt-catalyzed cyclization reaction for the synthesis of substituted indenoisoquinolinones was successfully extended to various substrates and the results are listed in Scheme 3. As indicated, reactions for substrates **3** with TMS substitution on the ethynal moiety afforded the corresponding desilylated indenoisoquinolinones **4b**–**4m** in moderate to good yields. Reactions for substituted *o*-bromobenzaldehyde with both electron-donating and electron-withdrawing groups were well-tolerated and provided the corresponding indenoisoquinolinones **4b**, **4c**, and **4f** in 61, 87, and 42% yields, respectively. Reactions for substrate **3** bearing electron-withdrawing or electron-donating groups were also compatible and afforded the corresponding products **4d** and **4e** in 65 and 85% yield, respectively. A variety of amines, including an aromatic amine with an electron-donating group, *p*-methoxybenzyl amine (PMB), and alkyl amines, are all reactive and the corresponding products **4g**–**4m** were obtained in moderate to good yields. When the TMS group on the ethynyl moiety of compound **3** was replaced by phenyl or *n*-butyl groups, the catalytic reactions still proceeded very well and the corresponding products **4n**–**4q** were provided in good to excellent yields. Apart from the NMR spectroscopic analysis, the structure of compound **4n** (Figure 1) was further verified by single-crystal X-ray diffraction.

The indenoisoquinolinones **4** could further be oxidized by SeO_2 to give the corresponding indenoisoquinoline-diones **5**, which were also known to be DNA topoisomerase I inhibitors. Thus, some selected indenoisoquinolinones were converted to their corresponding indenoisoquinoline-diones in nearly quan-



Scheme 3. Scope of the indenoisoquinolinones synthesis. Reaction conditions: compound **1** (0.6 mmol), compound **2** (0.6 mmol), compound **3** (0.3 mmol), [CoI_2(dppf)] (0.021 mmol, 7 mol%), dppf (0.021 mmol, 7 mol%), Zn (0.6 mmol), and $ZnCl_2$ (0.6 mmol) in MeCN (1 mL) at 100 °C for 20 h. Isolated yields are given in parenthesis. [a] Reactions were performed by using *o*-bromobenzaldimines.

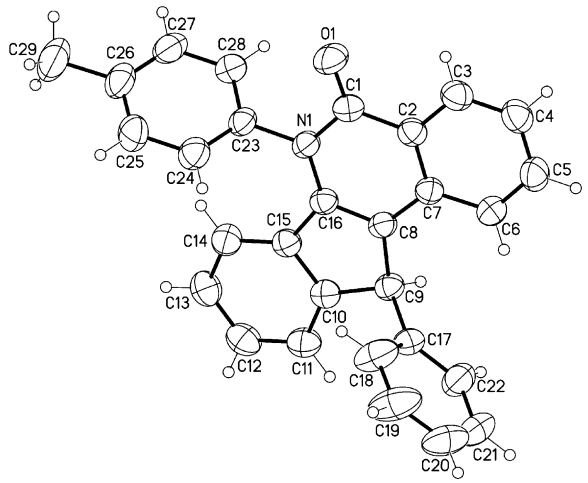
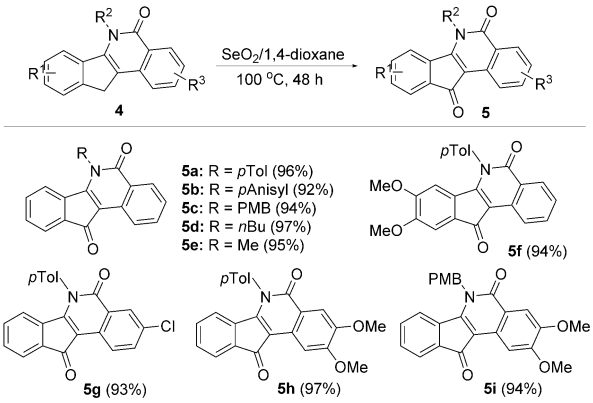


Figure 1. X-ray structure of compound **4n**. Ellipsoids are drawn at the 30% probability level.

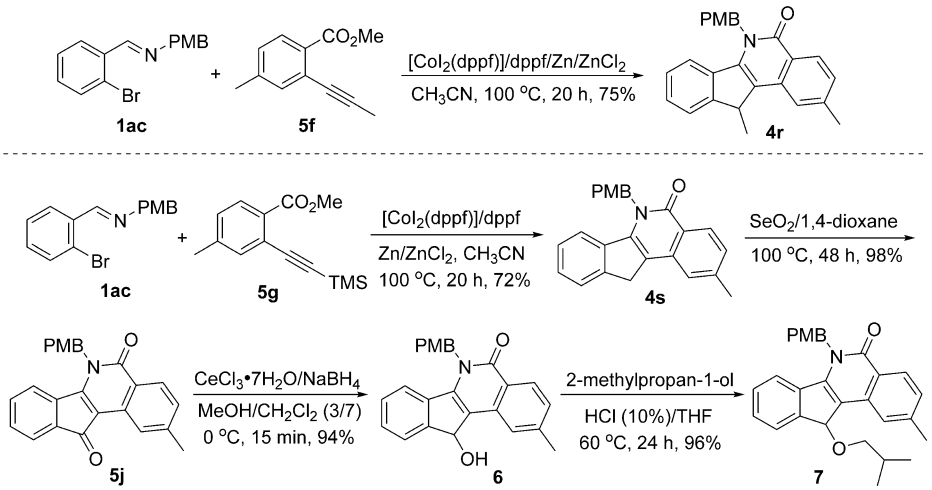
titative yields (Scheme 4). The reaction was carried out by using SeO_2 as the oxidant in 1,4-dioxane at 100 °C for 48 h to provide the desired indenoisoquinoline-diones.[5] This oxidation reaction cannot proceed at room temperature.



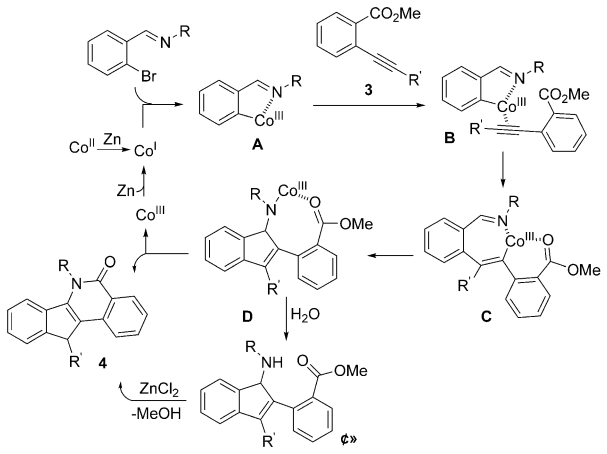
Scheme 4. Synthesis of the indenoisoquinoline-diones **5**. Reactions were performed with compounds **4** (0.30 mmol) and SeO_2 (2.40 mmol) in 1,4-dioxane (10 mL) at 100 °C for 48 h.

In order to extend the applications of this cobalt-catalyzed dual annulation reaction, two important pharmaceutical compounds **4r** and **7** were synthesized (Scheme 5). Compound **4r** was synthesized according to our developed protocol, which is known to enhance the differentiation of human myeloid leukemia cells when combined with all-*trans* retinoic acid (ATRA).[6] Compound **7** was prepared from compound **5j** using standard procedures, with further reduction of the carbonyl group and subsequent etherification with *i*BuOH. Compound **7** was reported to demonstrate significant cytotoxicity effects against four different tumor cell lines as well as Top 1 inhibitory activity.[3d] It is noteworthy that the syntheses of both compounds **4r** and **7** by using the present cobalt-catalyzed method appears to have the highest overall yields with the shortest synthetic steps.[1g,h]

A possible mechanism for the cobalt-catalyzed synthesis of indenoisoquinolinones **4** through a dual annulation reaction is shown in Scheme 6. The reaction is initiated by the reduction of Co^{II} to Co^{I} by zinc powder. Chelation-assisted oxidative insertion of Co^{I} into the aryl–bromine bond of *o*-bromobenzaldimine forms a five-membered ring, that is, the aza-cobaltacyle **A**. Coordination of alkyne **3** followed by regioselective insertion into the Co–C bond results in the formation of the aza-cobaltacycle **C**,[5,7] which is likely stabilized by the coordination of the carbonyl group. With the dppf ligand, this step is found to be crucial to give a single regioisomer product (see Scheme 6 for details). The regiochemistry for the insertion of alkyne in structure **B** in the present process is similar to that of the alkyne insertion to the five-membered azametallacycle intermediates in the reductive coupling reactions by using an imine and an alkyne.[8] In both cases, the aryl substituents of the aryl acetylenes are adjacent to the metal in the azametallacycle. A subsequently intramolecular nucleophilic addition to the imine group occurs to give intermediate **D**. Further nucleophilic addition of the N–Co bond to the ester group in the aza-cobalt complex **D** followed by elimination of the methoxyl group and a carbon–carbon double-bond migration in the indene core affords the final indenoisoquinolinone **4**. A similar acylation process with metal alkoxide elimination was proposed in the rho-



Scheme 5. Preparation of the biologically active indenoisoquinolinone derivatives **4r** and **7**.

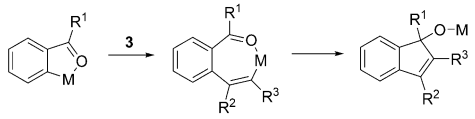


Scheme 6. Proposed mechanism for the formation of indenoisoquinolinones **4**.

dium- and cobalt-catalyzed nucleophilic addition reactions involving ester and vinyl methoxide groups.[9] Formation of Co^{I} through reduction of methoxycobalt(III) with zinc powder completes the catalytic cycle. Alternatively, intermediate **D** may be protonated to give indenamine **III**, which then undergoes a Lewis acid ($ZnCl_2$) assisted intramolecular lactamization to afford the final product **4**.

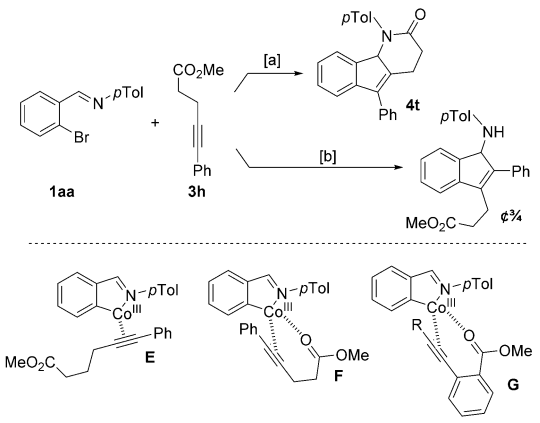
The unique behavior of the present cobalt-catalyzed reaction is interesting in view of the observation of the rhodium-, palladium-, nickel-, and ruthenium-mediated formation of isoquinoline or isoquinolinium salts from aza-metal complex **A** and an alkyne (Scheme 2).[3] Although rhodium and cobalt metals are in the same family and likely have the same oxidation state in the catalytic reaction, the resulting products are entirely different. A possible reason for the observed difference in the product formation of Co^{III} from the other metal catalysts is the acidity of Co^{III}. We expect that Co^{III} is a stronger Lewis acid than Rh^{III}, Pd^{II}, and Ni^{II} due to its smaller size or higher positive charge compared with the other three metal ions. Hence, the electrophilic insertion of an imine into the C–Co bond in the azametallacycle is more facile than to the other C–M bonds. It should be noted that all of the cobalt, nickel, palladium and rhodium metal–carbon bonds undergo 1,2-addition to the carbonyl group of aldehydes, ketones, or esters in carbocyclization reactions (Scheme 7).[10]

To understand the role and coordination ability of the ester group in the formation of intermediate **C** (Scheme 6), we ex-



Scheme 7. Electrophilic insertion of the carbonyl group to the vinyl–metal bond in carbocyclization reactions (M = Ni, Co, Pd, and Rh).

amined the product of the reaction of methyl 5-phenylpent-4-ynoate (**3h**) with imine **1aa** by using the different cobalt complexes [CoI_2(dppf)] and [CoI_2(dppe)]. Treatment of compound **1aa** with compound **3h** in the presence of [CoI_2(dppf)], dppf, Zn, and $ZnCl_2$ regioselectively gave the indenamine **VI** as the sole product in 70% yield. Product **VI** is likely formed by a regular addition of the M–C bond to the alkyne (Michael-type, Scheme 8). On the other hand, when [CoI_2(dppe)] was used as the catalyst, product **4t** was obtained in 58% yield. The regioselectivity of the alkyne insertion in the formation of compound **4t** is opposite to that of the general observation; that



Scheme 8. Reactions between compounds **1aa** and **3h** under various reaction conditions. a) [CoI_2(dppe)], dppe, Zn, $ZnCl_2$, CH_3CN, 100 °C. b) [CoI_2(dppf)], dppf, Zn, $ZnCl_2$, CH_3CN, 100 °C.

is, the electron-withdrawing substituent of the unsymmetrical alkyne should be situated next to the metal. This indicates that product **4t** might have arisen from an alkyne insertion induced by the sigma coordination of the ester group rather than an alkyne insertion based on the nature of the substituents. In the presence of the dppf ligand purely regioselective insertion of alkynes into azametallacycle **A** takes place, based on the alkyne polarity (intermediate **E**). The bulkiness of the dppf ligand seems to prevent the ester coordination. For dppe, the alkyne coordination is probably accompanied by ester coordination (intermediate **F**) leading to the formation of compound **4t**. For the catalytic reaction of methyl 2-ethynylbenzoate derivatives **3** with *o*-halobenzaldimine by using [CoI_2(dppf)] and dppf as the catalyst, intermediate **G** similar to intermediate **F** is likely involved during the catalytic reaction, in view of the observed product **4t** from compounds **1aa** and **3h** catalyzed by the same cobalt complex.

Conclusion

We have developed a new and efficient method for the synthesis of indenoisoquinolinones through a cobalt-catalyzed annulation reaction of methyl *o*-ethnylbenzoates with *o*-halobenzaldimines. It is a rare example of a catalytic tandem reaction involving a highly regioselective alkyne insertion followed by an intramolecular nucleophilic addition. Moreover, this method appears to provide the shortest synthetic route for the preparation of indenoisoquinolinones, and it is now possible to synthesize a series of structural analogues of bioactive indenoisoquinolinones with potentially medicinal properties.

Experimental Section

Synthesis of indenoisoquinolinone 4a: To a screw-caped seal tube, 2-bromobenzaldehyde **1a** (101 mg, 0.60 mmol) and *p*-toluidine **2a** (64 mg, 0.60 mmol) were added and the mixture was stirred at room temperature for 10 min. Then, to the reaction mixture were added [CoI_2(dppf)] (18 mg, 0.021 mmol), dppf (11.4 mg, 0.021 mmol), zinc (40 mg, 0.60 mmol), and zinc chloride (82 mg, 0.6 mmol) and the aperture of the seal tube was closed with a rubber septum. The tube was evacuated and purged three times with nitrogen gas. Methyl 2-((trimethylsilyl)ethynyl)benzoate **3a** (68 mg, 0.30 mmol) and freshly distilled acetonitrile (1.0 mL) were added to the mixture through a syringe. The septum was quickly exchanged for a screw cap and the reaction mixture was stirred at 100 °C for 20 h. At the end of the reaction, the reaction mixture was diluted with ethyl acetate and then filtered through a Celite-gel pad by using ethyl acetate as the eluent (≈20 mL). The combined filtrate was concentrated in vacuum and the residue was separated on a silica gel column by using a mixture of *n*-hexane and ethyl acetate as eluent to afford the desired pure white solid **4a** in 91% yield.

Acknowledgements

We thank the Ministry of Science and Technology of Republic of China (MOST, 102-2633M-007-002) for financial support of this research.

Keywords: azametallacycles · cobalt · indenes · isoquinoline · zinc

[1] a) J. M. Covey, C. Jaxel, K. W. Kohn, Y. Pommier, *Cancer Res.* **1989**, *49*, 5016–5022; b) A. Y. Chen, C. Yu, A. Bodley, L. F. Peng, L. F. Liu, *Cancer Res.* **1993**, *53*, 1332–1337; c) F. Zunino, G. Pratesi, *Expert Opin. Invest. Drugs* **2004**, *13*, 269–284; d) U. Vanhoefer, A. Harstrick, W. Achterrath, S. Cao, S. Seeber, Y. M. Rustum, *J. Clin. Oncol.* **2001**, *19*, 1501–1518; e) A. L. Ruchelman, S. K. Singh, A. Liu, N. Zhou, L. F. Liu, E. J. La Voie, *Lett. Drug Des. Discovery* **2004**, *1*, 198–202; f) M. Nagarajan, A. Morrell, A. Ioanoviciu, S. Antony, G. Kohlhagen, K. Agama, M. Hollingshead, Y. Pommier, M. Cushman, *J. Med. Chem.* **2006**, *49*, 6283–6289; g) W.-J. Cho, Q. M. Le, H. T. M. Van, K. Y. Lee, B. Y. Kang, E.-S. Lee, S. K. Lee, Y. Kwon, *Bioorg. Med. Chem. Lett.* **2007**, *17*, 3531–3534; h) A. Morrell, M. Jayaraman, M. Nagarajan, B. M. Fox, M. R. Meckley, A. Ioanoviciu, Y. Pommier, S. Antony, M. Hollingshead, M. Cushman, *Bioorg. Med. Chem. Lett.* **2006**, *16*, 4395–4399.

[2] a) G. Kohlhagen, K. D. Paull, M. Cushman, P. Nagafuji, Y. Pommier, *Mol. Pharmacol.* **1998**, *54*, 50–58; b) S. Antony, G. Kohlhagen, K. Agama, M. Jayaraman, S. Cao, F. A. Durrani, Y. M. Rustum, M. Cushman, Y. Pommier, *Mol. Pharmacol.* **2004**, *67*, 523–530; c) S. Antony, K. K. Agama, Z.-H. Miao, M. Hollingshead, S. L. Holbeck, M. H. Wright, L. Varticovski, M. Nagarajan, A. Morrell, M. Cushman, Y. Pommier, *Mol. Pharmacol.* **2006**, *70*, 1109–1120; d) M. S. Cushman, Y. G. Pommier, Int. Patent, WO 2004/100891A2, **2004**; e) A. Morrell, M. Placzek, S. Parmley, B. Grella, S. Antony, Y. Pommier, M. Cushman, *J. Med. Chem.* **2007**, *50*, 4388–4404.

[3] a) M. S. Cushman, A. E. Morrell, Y. G. Pommier, US patent, US 2006/0025595A1, **2006**; b) P. G. Jagtap, E. Baloglu, G. Southan, W. Williams, A. Roy, A. Nivorozhkin, N. Landrau, K. Desisto, A. L. Salzman, C. Szabó, *Org. Lett.* **2005**, *7*, 1753–1756; c) P. G. Jagtap, E. Baloglu, J. H. Van Duzer, C. Szabo, A. L. Salzman, Int. Patent, WO 03/020700A2, **2003**; d) H. T. M. Van, Q. M. Le, K. Y. Lee, E.-S. Lee, Y. Kwon, T. S. Kim, T. N. Le, S.-H. Lee, W.-J. Cho, *Bioorg. Med. Chem. Lett.* **2007**, *17*, 5763–5767; e) M. Cushman, T.-C. Choong, J. T. Valko, M. P. Koleck, *J. Org. Chem.* **1980**, *45*, 5067–5073; f) T. N. Le, S. G. Gang, W.-J. Cho, *Tetrahedron Lett.* **2004**, *45*, 2763–2766.

[4] a) C.-C. Liu, R. P. Korivi, C.-H. Cheng, *Chem. Eur. J.* **2008**, *14*, 9503–9506; b) R. P. Korivi, C.-H. Cheng, *Chem. Eur. J.* **2010**, *16*, 282–287; c) R. P. Korivi, Y.-C. Wu, C.-H. Cheng, *Chem. Eur. J.* **2009**, *15*, 10727–10731; d) R. P. Korivi, C.-H. Cheng, *Org. Lett.* **2005**, *7*, 5179–5182; e) Q. Huang, J. A. Hunter, R. C. Larock, *Org. Lett.* **2001**, *3*, 2973–2976, and references therein; f) D. Fischer, H. Tomeba, N. K. Pahadi, N. T. Patil, Y. Yamamoto, *Angew. Chem. Int. Ed.* **2007**, *46*, 4764–4766; *Angew. Chem.* **2007**, *119*, 4848–4850; g) N. Asao, S. Yudha, T. Nogami, Y. Yamamoto, *Angew. Chem. Int. Ed.* **2005**, *44*, 5526–5528; *Angew. Chem.* **2005**, *117*, 5662–5664; h) R. Yanada, S. Obika, H. Kono, Y. Takemoto, *Angew. Chem. Int. Ed.* **2006**, *45*, 3822–3825; *Angew. Chem.* **2006**, *118*, 3906–3909; i) N. Guimond, K. Fagnou, *J. Am. Chem. Soc.* **2009**, *131*, 12050–12051; j) N. Senthilkumar, P. Gandeepan, J. Jayakumar, C.-H. Cheng, *Chem. Commun.* **2014**, *50*, 3106–3108; k) S.-C. Chuang, P. Gandeepan, C.-H. Cheng, *Org. Lett.* **2013**, *15*, 5750–5753.

[5] a) W. J. Hoekstra in *Oxidizing and Reducing Agents* (Eds.: S. D. Burke, R. L. Danheiser), Wiley, New York, **2000**, pp. 358–359.

[6] a) S. H. Kim, S. M. Oh, J. H. Song, D. Cho, Q. M. Le, S.-H. Lee, W.-J. Cho, T. S. Kim, *Bioorg. Med. Chem.* **2008**, *16*, 1125–1132.

[7] For azametallacycles, see: a) C.-H. Yeh, R. P. Korivi, C.-H. Cheng, *Angew. Chem. Int. Ed.* **2008**, *47*, 4892–4895; *Angew. Chem.* **2008**, *120*, 4970–4973; b) S. Ogoshi, H. Ikeda, H. Kurosawa, *Angew. Chem. Int. Ed.* **2007**, *46*, 4930–4932; *Angew. Chem.* **2007**, *119*, 5018–5020.

[8] a) S. J. Patel, T. F. Jamison, *Angew. Chem. Int. Ed.* **2003**, *42*, 1364–1367; *Angew. Chem.* **2003**, *115*, 1402–1405; b) S. J. Patel, T. F. Jamison, *Angew. Chem. Int. Ed.* **2004**, *43*, 3941–3944; *Angew. Chem.* **2004**, *116*, 4031–4034.

[9] a) D. K. Rayabarapu, H.-T. Chang, C.-H. Cheng, *Chem. Eur. J.* **2004**, *10*, 2991–2996; b) T. Miura, T. Sasaki, H. Nakazawa, M. Murakami, *J. Am. Chem. Soc.* **2005**, *127*, 1390–1391; c) T. Miura, M. Shimada, M. Murakami, *J. Am. Chem. Soc.* **2005**, *127*, 1094–1095; d) T. Miura, T. Sasaki, T. Harumashi, M. Murakami, *J. Am. Chem. Soc.* **2006**, *128*, 2516–2517.

[10] a) D. K. Rayabarapu, C.-H. Cheng, *Chem. Commun.* **2002**, 942 – 943; b) D. K. Rayabarapu, C.-H. Yang, C.-H. Cheng, *J. Org. Chem.* **2003**, *68*, 6726 – 6731; c) K.-J. Chang, D. K. Rayabarapu, C.-H. Cheng, *Org. Lett.* **2003**, *5*, 3963 – 3966; d) K.-J. Chang, D. K. Rayabarapu, C.-H. Cheng, *J. Org. Chem.* **2004**, *69*, 4781 – 4787; e) L. G. Quan, V. Gevorgyan, Y. Yamamoto, *J. Am. Chem. Soc.* **1999**, *121*, 3545 – 3546; f) R. Shintani, K. Okamoto, T. Hayashi, *Chem. Lett.* **2005**, *34*, 1294 – 1295.

Received: March 24, 2015
Published online on May 18, 2015